

U.S. Application No.: 09/884,526
Attorney Docket No. 07680.0019-00000

IN THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A method of reducing the accumulation of globotriaosylceramide in a subject diagnosed as having Fabry disease comprising administering to the subject a therapeutically effective amount of two or more of the following:

- a) an exogenously produced natural or recombinant α -galactosidase A,
- b) a viral or non-viral vector encoding a α -galactosidase A, and
- c) a small molecule that inhibits upstream generation of lysosomal

hydrolase substrate,

such that the accumulation of globotriaosylceramide in the subject is reduced.

2. (Withdrawn) The method according to claim 1 wherein the combination therapy comprises alternating between administration of an enzyme replacement therapy and a small molecule therapy.

3. (Withdrawn) The method according to claim 1 wherein the combination therapy comprises simultaneously administering an enzyme replacement therapy and a small molecule therapy.

4. (Currently amended) The method according to claim 1, wherein the combination therapy comprises administering

- a) a viral or non-viral vector encoding α -galactosidase A and

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b) one of the following: an exogenously produced natural α -galactosidase

A, a recombinant α -galactosidase A and a small molecule that inhibits upstream generation of lysosomal hydrolase substrate.

5. (Canceled)

6. (Previously presented) The method according to claim 1 wherein the α -galactosidase A is a recombinant α -galactosidase A.

7. (Withdrawn) The method according to claim 1 wherein the small molecule is deoxynojirimycin or a deoxynojirimycin derivative.

8. (Withdrawn) The method according to claim 7, wherein the deoxynojirimycin derivative is N butyldeoxynojirimycin (NB-DNJ) or N-(5-adamantane-1-yl-methoxy)pentyl-deoxynojirimycin (AMP-DNJ).

9. (Withdrawn) The method according to claim 1, wherein the small molecule comprises an effective amount of a D-*threo*-1-phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (P4) derivative.

10. (Withdrawn) The method according to claim 9, wherein the P4 derivative is D-*threo*-1-(3',4'-ethylenedioxy)phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (D-t-et-P4).

11. (Withdrawn) The method according to claim 1, wherein Fabry disease has at least one central nervous system manifestation and the small molecule therapy comprises AMP-DNJ.

12. (Withdrawn) The method according to claim 1, comprising administering a therapeutically effective amount of an exogenously produced

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natural or recombinant α -galactosidase A and a small molecule such that the Fabry disease is treated.

13. (Previously presented) The method of claim 1, wherein the viral or non-viral vector encoding a α -galactosidase A is administered before the exogenously produced natural or recombinant α -galactosidase A.

14. (Previously presented) The method of claim 1, wherein the exogenously produced natural or recombinant α -galactosidase is administered before the viral or non-viral vector encoding a α -galactosidase A.

15. (Previously presented) The method of claim 1, wherein the exogenously produced natural or recombinant α -galactosidase is administered simultaneously with the viral or non-viral vector encoding a α -galactosidase A.

16. (Previously presented) The method of claim 1, wherein the exogenously produced natural or recombinant α -galactosidase is administered alternately with the viral or non-viral vector encoding a α -galactosidase A.

17. (Previously presented) The method of claim 1, wherein the exogenously produced natural or recombinant α -galactosidase is administered intravenously.

18. (Previously presented) The method of claim 1, wherein the viral or non-viral vector encoding a α -galactosidase A is administered ex vivo.

19. (Previously presented) The method of claim 1, wherein the viral or non-viral vector encoding a α -galactosidase A is administered in vivo.